

CLAIMS

1. A polypeptide having brain-localizing activity, wherein 10% or more of the polypeptide is comprised of basic amino acid residues (K or R).

5 2. A polypeptide having brain-localizing activity, wherein the polypeptide comprises a cyclic peptide region, and wherein 10% or more of the cyclic peptide region is comprised of basic amino acid residues (K or R).

10 3. A polypeptide having brain-localizing activity, wherein the polypeptide comprises a cyclic peptide region and at least one or more basic amino acid residues (K or R) in the cyclic peptide region.

4. A polypeptide having brain-localizing activity, wherein the polypeptide comprises a cyclic peptide region and at least one or more basic amino acid residues (K or R), and wherein 80% or more of the remaining amino acid residues in the cyclic region are selected from the following group of amino acid residues:

15 G, A, V, L, S, T, P, Q, H, and N.

5. A polypeptide having brain-localizing activity, wherein the polypeptide comprises the amino acid motif sequence of:

$X_1-(R \text{ or } K)-X_3-X_4$ or

$X_4-X_3-(R \text{ or } K)-X_1$,

20 wherein X_1 denotes S, T, N, P, V, or L; X_3 denotes an arbitrary amino acid; and X_4 denotes G, S, T, C, N, L, Q, or Y.

6. The polypeptide of any one of claims 2 to 4, wherein the cyclic peptide region comprises the amino acid motif sequence of claim 5.

7. The polypeptide of claim 5 or 6, wherein the amino acid motif sequence is:

25 $X_1-(R \text{ or } K)-X_3-X_4$ or

$X_4-X_3-(R \text{ or } K)-X_1$,

wherein X_1 denotes S, T, N, P, or V; X_3 denotes an arbitrary amino acid; and X_4 denotes an uncharged polar amino acid (G, S, T, C, N, Q, or Y).

8. The polypeptide of claim 5 or 6, wherein the amino acid motif sequence is:

30 $X_1-(R \text{ or } K)-X_3-X_4$ or

$X_4-X_3-(R \text{ or } K)-X_1$,

wherein X_1 denotes S, T, P, or L; X_3 denotes an arbitrary amino acid; and X_4 denotes S, T, C, L, or Q.

9. The polypeptide of any one of claims 1 to 8, wherein the polypeptide has transmigration-inducing activity.

10. The polypeptide of any one of claims 1 to 8, wherein the polypeptide has activity

to bind to a cerebrovascular endothelial cell.

11. A polypeptide of any one of (a) to (c) described below:

(a) a polypeptide comprising the amino acid sequence of any one of SEQ ID NOs: 1 to 12;

(b) a polypeptide comprising a peptide region cyclized by a disulfide bond formed between cysteine residues on both ends of the polypeptide of (a); and

(c) a polypeptide having brain-localizing activity, and comprising an amino acid sequence with one or several amino acid additions, deletions, or substitutions in the amino acid sequence of any one of SEQ ID NOs: 1 to 12.

12. The polypeptide of any one of claims 1 to 11, wherein the length of the polypeptide is 9 amino acids or less.

13. A polynucleotide encoding the polypeptide of any one of claims 1 to 12.

14. An antibody that binds to the polypeptide of any one of claims 1 to 12.

15. A pharmaceutical agent for conferring brain-localizing activity to an arbitrary molecule, wherein the agent comprises the polypeptide of any one of claims 1 to 12.

16. The pharmaceutical agent of claim 15, wherein the arbitrary molecule is an arbitrary polypeptide.

17. A molecule having brain-localizing activity, wherein the molecule comprises the polypeptide of any one of claims 1 to 12.

18. The molecule of claim 17, wherein the molecule is a phage particle or a coat protein of a phage particle.

19. The molecule of claim 17, wherein the molecule is a fusion protein formed with the polypeptide of any one of claims 1 to 12.

20. A carrier for delivery to the brain, wherein the carrier comprises the polypeptide of any one of claims 1 to 12.

21. A carrier for delivery to the brain, wherein the carrier comprises a structure in which the polypeptide of any one of claims 1 to 12 is bound to a micelle, liposome, or microcapsule.

22. A therapeutic agent for brain disease, wherein the agent comprises a structure in which a drug is supported by the carrier of claim 20 or 21.

23. A method for producing a molecule having brain-localizing activity, wherein the method comprises binding the polypeptide of any one of claims 1 to 12 to an arbitrary molecule.

24. A method for producing a protein molecule having brain-localizing activity, wherein the method comprises the steps of:

(a) preparing an expression vector comprising a DNA in an expressible manner, wherein the DNA has a structure in which a DNA encoding an arbitrary protein molecule is linked to a

DNA encoding the polypeptide of any one of claims 1 to 12;

(b) introducing the expression vector into a cell; and

(c) collecting an expression product of the vector.

5 25. A method for translocating an arbitrary molecule into the brain of a non-human animal, wherein the method comprises the steps of:

(a) producing a molecule having brain-localizing activity, wherein the molecule comprises a structure in which an arbitrary molecule is bound to the polypeptide of any one of claims 1 to 12; and

(b) administering the molecule into the body of the non-human animal.

10 26. A method of screening for a molecule having binding activity to the polypeptide of any one of claims 1 to 12, wherein the method comprises the steps of:

(a) contacting the polypeptide of any one of claims 1 to 12 with a test molecule;

(b) detecting binding activity between the polypeptide and the test molecule; and

(c) selecting a molecule that binds to the polypeptide.

15 27. A method of screening for a polypeptide having brain-localizing activity, wherein the method comprises the steps of:

(a) preparing a phage particle displaying a test polypeptide on its phage coat protein;

(b) administering the phage particle to a non-human animal;

(c) collecting a phage particle from a brain tissue of the non-human animal; and

20 (d) selecting a test polypeptide displayed on the phage particle collected in step (c) as a polypeptide having brain-localizing activity.

28. The method of claim 27, wherein the test polypeptide comprises the amino acid motif sequence of any one of claims 5, 7, and 8.

29. The method of claim 27, wherein the phage is M13 phage or T7 phage.

25 30. The method of claim 27, wherein the method further comprises selecting a phage particle that binds to a cerebrovascular endothelial cell subsequent to step (a).